

ATTACHMENT A - NEW CLAIMS

CLAIMS

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--22. An active ingredient matrix: in the form of a biologically resorbable, porous nonwoven of collagen fibrils in lyophilized form with a retarded release of active ingredients, containing at least one homogeneously distributed active ingredient poorly soluble in water and body fluids, which, apart from the collagen fibrils as the carrier structure and the at least one active ingredient, is substantially free from further constituents, which is substantially free from salt and in which the at least one active ingredient in physiological medium has a solubility of < 10 mg/ml.

23. The active ingredient matrix according to claim 22, wherein it has a layer thickness of 0.5 to 15 mm.

24. The active ingredient matrix according to claim 22, wherein it has a density of 12 to 180 mg/cm³.

25. The active ingredient matrix according to claim 22, wherein it has a pore volume of 60 to 80% of the total volume.

26. The active ingredient matrix according to claim 22 wherein it has an average pore size in the range of 20 to 150 μ m.

27. The active ingredient matrix according to claim 22 wherein it has an air permeability of 2500 to 5000 ml/cm²/min for a layer thickness of 4.2 mm.

28. The active ingredient matrix according to claim 22, wherein the at least one poorly soluble active ingredient is a medicament.

29. The active ingredient matrix according to claim 28, wherein the medicament is an antibiotic.

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30. The active ingredient matrix according to claim 22 wherein in addition to the at least one poorly soluble active ingredient, it contains at least one less poorly soluble or easily soluble active ingredient.

31. A method for the manufacture of biodegradable active ingredient matrix in the form of an open-cell nonwoven or sponge of uncrosslinked, resorbable collagen fibrils, for the manufacture of an active ingredient matrix according to claim 22, wherein pieces of cleaned, degreased and dried hide are allowed to swell in dilute, aqueous solutions of organic acids until an elastic material is

obtained, the swollen pieces are rinsed several times with aqueous media, until the pH-value is increased, the rinsed pieces are mechanically separated into fibers for forming a suspension of collagen fibrils, the pourable collagen suspension having a pH-value of > 3.5 to < 4.8 is mixed with at least one difficultly soluble active ingredient in finely divided form and homogenized and the active ingredient-containing suspension is then lyophilized to the nonwoven or sponge.

32. The method according to claim 31, wherein the concentration of the organic acid used for swelling and the number of rinsing operations are chosen and matched to one another in such a way that following the rinsing and separation into fibers, without prior pH-correction, a collagen suspension is obtained with a pH-value of > 3.5 to < 4.8 .

33. The method according to claim 31, wherein the rinsing operation covers at least two rinsing cycles.

34. The method according to claim 32, wherein rinsing is performed for 5 to 60 hours.

35. The method according to claim 32, wherein for swelling purposes use is made of an acid solution with an acid concentration of 0.01 to 2 N.

36. The method according to claim 32, wherein the hide portions are swollen in the organic acid to 3 to 10 times their weight.

37. The method according to claim 32, wherein after rinsing and removing the rinsing water, the swollen collagen granulate is transformed by the addition of water into a 0.1 to 10 % mixture, based on the dry collagen material weight and this mixture is homogenized by dispersion to the collagen suspension, the fiber union of the collagen fibrils being broken.

38. The method according to claim 32, wherein the at least one poorly soluble active ingredient is added in finely divided form.

39. The method according to claim 32, wherein the suspension of the collagen fibrils, following the addition of the at least one difficultly soluble active ingredient, is homogenized for uniform distribution of the at least one active ingredient in the suspension.

40. The method according to claim 32, wherein apart from the at least one difficultly soluble active ingredient, at least one less poorly soluble active ingredient is added.

41. The method according to claim 32, wherein the homogenized, active ingredient-containing collagen suspension is lyophilized without any further intermediate treatment to areal nonwovens.

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42. Use of the active ingredient matrix according to claim 22 as an implantable and completely resorbable depot for active ingredients with a retarded active ingredient delivery.

43. The active ingredient matrix according to claim 23, wherein the layer thickness is 2 to 5 mm.

44. The active ingredient matrix according to claim 27, wherein the air permeability is 2700 to 3400 ml/cm²/min.

45. The active ingredient matrix according to claim 28, wherein the antibiotic is one or more of aminoglycoside antibiotics.

46. The active ingredient matrix according to claim 45, wherein the aminoglycoside antibiotics are selected from the group of clindamicin-palmitate, clindamicin-palmitate hydrochloride and gentamicin-crobecfat.

47. The method according to claim 31, wherein the aqueous medium is demineralized water.

48. The method according to claim 32, wherein the pH-value is 4 to 4.5.

49. The method according to claim 33, wherein the rinsing operation covers at least five rinsing cycles.

50. The method according to claim 34, wherein rinsing is performed for 6 to 48 hours.

51. The method according to claim 35, wherein the acid concentration is 0.05 to 0.5 N.

52. The method according to claim 36, wherein the hide portions are swollen to 4 to 8 times their weight.

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53. The method according to claim 38, wherein the active ingredient is suspended in an aqueous medium.

54. The method according to claim 40, wherein the less poorly soluble active ingredient has the same kind of activity .

55. The method according to claim 41, wherein the collagen suspension is lyophilized to sponges.

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